Diagnosing melanoma: the method matters

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Accurate diagnosis and staging of invasive melanoma requires an appropriate biopsy and technical proficiency

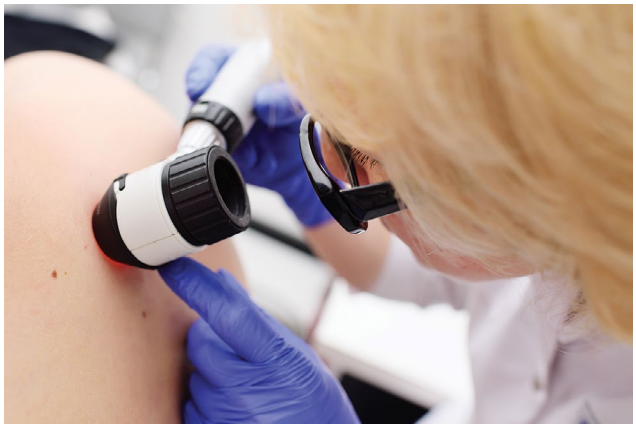
Tumour base transection during shave biopsy remains a clinically significant problem when diagnosing melanoma. In this issue of the Journal, de Menezes and her colleagues[1] report that the number of shave biopsies in Victoria has more than doubled over the past 10 years, a major concern for clinicians and their patients. Excisional biopsy is the preferred method for assessing melanoma, as invasion is often impossible to predict pre-operatively; excision minimises the risks of delayed or misdiagnosis and inaccurate tumour staging.

Shave biopsy is widely used in skin cancer practice. The relative merits and risks of shave biopsies for sampling melanocytic lesions have been debated for decades, but recent advances in melanoma staging,[2] together with unprecedented access to highly effective adjuvant systemic therapies,[3–5] require us to revisit this contentious question.

In the first population-based study of changes in the incidence of partial biopsy techniques for diagnosing invasive melanoma, de Menezes and her co-authors found that the proportion of shave biopsies for diagnosing invasive melanoma increased from 9% in 2005 to 20% in 2015.[1] This illustrates the widening divide between current clinical practice and the recommendations of our national, evidence-based guidelines, which specifically warn of the dangers of partial biopsy, including shave biopsy, for diagnosing invasive melanoma.[6] These include the increased risk of misdiagnosing a melanoma as a benign tumour (in one large study estimated to be 4.5% for shave biopsies, 1.7% for excisional biopsy[7]) and inaccurate staging of diagnosed melanomas.[6]

Why base transection matters

Melanoma base transection is common in shave biopsies, the incidence ranging from 9% to 68%.[8–13] Breslow tumour thickness (vertical depth of invasion) is the single most important prognostic characteristic of the primary tumour; it guides determination of the definitive resection margins and informs decisions about the appropriateness of sentinel lymph node biopsy (SLNB). Discussing the role of SLNB with patients is often difficult, as the evidence regarding this intervention is complex;[6] it takes time and careful explanation for patients to properly comprehend the potential benefits and implications (including potential access to systemic therapies) and the prognostic information it provides. Inaccurate Breslow thickness estimation, not infrequent with shave biopsies[14–16] adds significantly to patient uncertainty and the psychological stress of difficult treatment discussions. The findings of the Multicenter Selective



Lymphadenectomy Trial II[17] have led to a rapid change in clinical practice; completion lymph node dissection is no longer the routine choice for patients with a positive SLNB. In addition, we now have highly effective systemic adjuvant therapies, including targeted or immune therapies for patients with resected stage III melanoma,[3–5] and SLNB has become the gateway to potentially life-saving adjuvant therapies for many patients.

The new melanoma staging system (in the eighth edition of the American Joint Committee on Cancer staging manual)[18] uses both primary tumour and nodal characteristics to sub-categorise patients with stage III disease. Five-year survival varies considerably by stage III subcategory, ranging from 93% for IIIA to 32% for IIID.[19] Accurate staging allows more precise prognostication, which is essential for determining the absolute risk reduction achievable with systemic therapy, and provides the basis of discussions with patients about potential treatment benefit and the risks of adverse events. Inaccurate T-staging based on underestimation of Breslow thickness resulting from base transection during a shave biopsy significantly confounds treatment decisions, and for some patients it can also be a barrier to effective therapies or clinical trials, potentially making it a question of medico-legal liability in the future.

The clinical significance of tumour base transection is often assessed by examining the frequency with which residual tumour is identified in the definitive wide local excision specimen; estimates range between 3.5% and 44%.[11,14–16] Mechanical, surgical, and inflammatory processes at the wound site can destroy tumour cells, and reparative changes, including inflammation and fibrosis, are inevitable at the biopsy site. For these reasons, the true tumour thickness cannot be reliably calculated by summing the melanoma thicknesses of all specimens.[18] Other attempts to measure the clinical impact of base transection have explored the relationship between biopsy type and survival in retrospective analyses of pooled data sets.[12,20,21] These studies did not find that a survival disadvantage for patients with base transection, but their results reflect outcomes before effective adjuvant systemic

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therapy had been introduced and cannot be extrapolated to current melanoma practice. Further, none of these studies examined the impact of the increased risk of delayed diagnosis or misdiagnosis of melanoma associated with shave biopsy.

Good clinical practice requires individualisation of care, and excision biopsy is not practical or appropriate for sampling all pigmented lesions in all patients. For example, clinical suspicion of lentigo maligna may be an indication for partial shave biopsy, despite the risk of base transection of an invasive component, as it allows examination of a larger epidermal area for diagnostic purposes before embarking upon complex surgery.

The difference between shave excision and shave biopsy lies in the differing intentions of the treating clinician, and retrospective studies are limited by the inability to know the intent of an individual biopsy. De Menezes and colleagues[1] found that the deep margin was not transected in about half the shave biopsies assessed, suggesting differences in the technical proficiency of practitioners who performing them. This possibility could not be examined in this study, but could be considered in future studies.

Why is shave biopsy being used more?

De Menezes and her co-authors found that the diagnosis of invasive melanomas by shave biopsy had significantly increased among all Victorian clinicians, both specialist and general practitioners. This raises the important public health question of why clinical practice is increasingly diverging from the national guidelines. Although it is widely believed that shave biopsy has fewer adverse effects and achieves better cosmesis than excisional biopsy, such assertions are not supported by clinical studies. The undisputed features of shave biopsy are that it is faster, requires less surgical material, does not require follow-up for suture removal, and is less expensive for both the patient and the medical practice than excisional biopsy. Well designed prospective trials are needed to better understand the impact of shave biopsies, and analysing validated patient-reported outcomes would facilitate assessment of the patient experience.

When melanoma is suspected, we recommend that the treating clinician prefer excision with a narrow margin and primary closure, in keeping with the Australian guidelines,[6] as this is more likely to ensure accurate diagnosis and microstaging than partial biopsy.

Competing interests: Jonathan Stretch, Richard Scolyer and Pascale Guitera are involved in developing the Cancer Council wiki guidelines.

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1 de Menezes SL, Kelly JW, Wolfe R, et al. The increasing use of shave biopsy for diagnosing invasive melanoma in Australia. *Med J Aust* 2019; 211: 213–218.

2 Gershenwald JE, Scolyer RA, Hess KR, et al; American Joint Committee on Cancer Melanoma Expert Panel, International Melanoma Database and Discovery Platform. Melanoma staging: evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin* 2017; 67: 472–492.

3 Long GV, Hauschild A, Santinami M, et al. Adjuvant dabrafenib plus trametinib in stage III BRAF-mutated melanoma. *N Engl J Med* 2017; 377: 1813–1823.

4 Eggermont AMM, Blank CU, Mandala M, et al. Adjuvant pembrolizumab versus placebo in resected stage III melanoma. *N Engl J Med* 2018; 378: 1789–1801.

5 Weber J, Mandala M, Del Vecchio M, et al. American Joint Committee on Cancer Melanoma Expert Panel, International Melanoma Database and Discovery Platform. Adjuvant nivolumab versus ipilimumab in resected stage III or IV melanoma. *N Engl J Med* 2017; 377: 1824–1835.

6 Cancer Council Australia Melanoma Guidelines Working Party. Clinical practice guidelines for the diagnosis and management of melanoma. Updated Apr 2019. https://wiki.cancer.org.au/australiawiki/index.php?oldid=201397 (viewed May 2019).

7 Ng JC, Swain S, Dowling JP, et al. The impact of partial biopsy on histopathologic diagnosis of cutaneous melanoma: experience of an Australian tertiary referral service. *Arch Dermatol* 2010; 146: 234–239.

8 Egnatios GL, Dueck AC, Macdonald JB, et al. The impact of biopsy technique on upstaging, residual disease, and outcome in cutaneous melanoma. *Am J Surg* 2011; 202: 771–777.

9 Hieken TJ, Hernández-Irizarry R, Boll JM, Jones Coleman JE. Accuracy of diagnostic biopsy for cutaneous melanoma: implications for surgical oncologists. *Int J Surg Oncol* 2013; 2013: 196493.

10 Lowe M, Hill N, Page A, Delman KA. The impact of shave biopsy on the management of patients with thin melanomas. *Am Surg* 2011; 77: 1050–1053.

11 Mills JK, White I, Diggs B, et al. Effect of biopsy type on outcomes in the treatment of primary cutaneous melanoma. *Am J Surg* 2013; 205: 585–590.

12 Mir M, Chan CS, Khan F, at al. The rate of melanoma transection with various biopsy techniques and the influence of tumor transection on patient survival. *J Am Acad Dermatol* 2013; 68: 452–458.

13 Zager JS, Hochwald SN, Marzban SS, et al. Shave biopsy is a safe and accurate method for the initial evaluation of melanoma. *J Am Coll Surg* 2011; 212: 454–460.

14 Kaiser S, Vassell R, Pinckney RG, at al. Clinical impact of biopsy method on the quality of surgical management in melanoma. *J Surg Oncol* 2014; 109: 775–779.

15 Saco M, Thigpen J. A retrospective comparison between preoperative and postoperative Breslow depth in primary cutaneous melanoma: how preoperative shave biopsies affect surgical management. *J Drugs Dermatol* 2014; 13: 531–536.

16 Moore P, Hundley J, Levine EA, at al. Does shave biopsy accurately predict the final Breslow depth of primary cutaneous melanoma? *Am Surg* 2009; 75: 369–373.

17 Faries MB, Thompson JF, Cochran AJ, et al. Completion dissection or observation for sentinel-node metastasis in melanoma. *N Engl J Med* 2017; 376: 2211–2222.

18 Gershenwald JE, Scolyer RA, Hess KR, et al. Melanoma of the skin. In: Amin MB, Edge SB, Greene FL, editors. AJCC cancer staging manual. Cham: Springer International, 2017; pp. 563–585.

19 Gershenwald JE, Scolyer RA. Melanoma staging: American Joint Committee on Cancer (AJCC) 8th edition and beyond. *Ann Surg Oncol* 2018; 25: 2105–2110.

20 Molenkamp BG, Sluijter BJ, Oosterhof B, at al. Non-radical diagnostic biopsies do not negatively influence melanoma patient survival. *Ann Surg Oncol* 2007; 14: 1424–1430.

21 Martin RC, Scoggins CR, Ross MI, et al. Is incisional biopsy of melanoma harmful? *Am J Surg* 2005; 190: 913–917. ■